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BY T. LEWIS AND A. N. DRURY.

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THE EFFECT OF VAGAL STIMULATION ON INTRA-AURICULAR BLOCK PRODUCED BY PRESSURE OR COOLING.*

By T. LEWIS and A. N. DRURY.

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Historical.

IN 1883, Gaskell⁵ reported his experiments upon the tortoise auricle. He slit up the auricle so as almost to divide it into two parts, the one attached to the sinus, the other to the ventricle, these two parts being left united at one point by a narrow bridge of muscle tissue. If the bridge is rendered sufficiently narrow, it becomes incapable of conveying each impulse from the spontaneously beating basal portions of the preparation; the bridge constitutes a point of block. Gaskell tested the effects of vagal stimulation upon this block. He states that right and left vagus possess the power of removing a partial block. He writes: "This improvement of conduction power is, like the improvement in the force of the contractions or the after-acceleration, spread over a long period of time, so that in most cases stimulation of the nerve removes the partial block altogether." Again, he states, "every second contraction passes before the stimulation, then during and after the nerve stimulation every contraction passes, and then again in a very short time only every second contraction is able to pass." Still later he states, "I possess but few curves which show unmistakably any diminution of conduction power in consequence of nerve stimulation. Still, as Figs. 12 and 13, Pl. IV., show, such an increase in the extent of the block does undoubtedly sometimes occur."

To be understood, these statements require further examination. The decrease of the original block *during* vagal stimulation, which Gaskell saw, was accompanied by a lowering of the rate of sinus beating and resulted from this lowered rate of beating, the longer rests and consequent greater recovery of the tissue bridge between the beats. Where there was no decrease, or no

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appreciable decrease, in the rate of sinus beating under vagal stimulation, the block was increased, as his curves clearly show. In these descriptions of Gaskell's experiments there is no evidence to show that during vagal stimulation the tissue of the bridge is capable of conducting impulses more effectively than before the nerve stimulation was applied, the improvement of conduction which he here describes is not the direct outcome of vagal stimulation, but is secondary to a change of rate. Two figures which he uses as illustrations show no change of sinus rate, and in both these nerve stimulation produces a greatly enhanced block. It is here to be observed, however, that in his subsequent remarks, Gaskell refers to instances in which, though the rate was not reduced, the block became decreased. Since these instances are not illustrated, it does not seem to us entirely clear that the block was relieved actually during the stimulation, though this is the actual statement in the text. It seems to us that Gaskell is probably here describing the effects immediately following nerve stimulation.

Such effects are perfectly clearly illustrated and described in other places. The usual effect of vagal stimulation, when a partial block has been established, is a lowered rate of sinus beating and the passage of the bridge by each impulse *during* stimulation; immediately stimulation is withdrawn there is a rebound from inhibition, and the beats of the sinus, now accelerated, pass the bridge regularly and for considerable periods of time.

From Gaskell's description of the tortoise auricle therefore, it is quite clear that vagal stimulation may decrease the conduction power of the bridge; it is equally clear that the original block usually becomes reduced as an immediate *after effect* of stimulation; it is not quite clear if, in exceptional cases, he saw an actual increase in the bridge's capacity to conduct *during* vagal stimulation.

Gaskell's observations are summed up in his sentence:—"Although the initial effect of the vagus is to depress some function, its final and most enduring power is to exalt, intensify and repair that function."

In Engelmann's experiments³ a clamp was applied to the auricle, and the interval between the contractions of the proximal and distal segments was measured. These experiments afford little information from our present standpoint, as little or no change of interval was observed during stimulation, and for the most part vagal stimulation produced much slowing of the heart.

Garrey⁴ used the turtle's heart. He produced intra-auricular block by applying a clamp between the right and left auricle and obtained results with vagal stimulation, which he describes as invariable. When he stimulated the left nerve and obtained no alteration of basal rate, the block was always increased; when he stimulated the right nerve and obtained little reduction of rate, a similar effect was observed; when on stimulating the right nerve, the basal rate was much reduced, the degree of block diminished. Garrey's experiments, and his discussion of them, particularly emphasise the double influence of the vagus, its direct and depressing effect

on the one hand, its effect of relieving block indirectly by reducing the rate at which impulses impinge on the bridge, on the other.

To sum up, so far as the cold-blooded auricle is concerned, there is definite and unanimous evidence that vagal stimulation will further decrease the power of conduction when this is originally lowered by clamping, or by other injury. There is insufficient evidence that the reverse effect occurs, though certain of Gaskell's statements may be read to imply that this reversed action is sometimes seen.

So far as the mammalian auricle is concerned, we are aware of few observations. It has been shown by Lewis, Meakins, and White,¹¹ and more recently and conclusively by Lewis, Drury, and Bulger,³ that the rate of conduction in the uninjured dog's auricle, beating at normal rates, is uninfluenced by vagal stimulation (right or left). But it was shown by the same workers⁸ that when the rate of conduction is lowered as a consequence of raised rate of beating, that vagal stimulation in these circumstances invariably improves conduction, increasing the rate until it reaches its original value. Similar observations have been made on the intra-auricular block produced by strophanthin poisoning.⁹ Both these effects have been attributed to a reduction of the refractory period of the auricle under vagal stimulation. A similar effect of vagal stimulation is observed when conduction in the auricle is retarded as a consequence of quinidine poisoning, though the nature of this reaction is less clear.¹⁰

In view of these observations we decided to test changes in conduction in the auricle under vagal stimulation more extensively, and first describe our observations upon intra-auricular block produced by compression. These were intended primarily to test the question as to whether there is an essential difference between the action of the vagus in intra-auricular block produced by compression or similar damage, in the cold and warm-blooded heart.

Observations on block produced by compression.

The auricular appendages are parts of the auricle, which are peculiarly suited to observations such as are to be described, for they form natural projections which may be compressed at their bases without unduly interfering with the circulation. The experiments to be described were performed upon the right appendix almost exclusively.* Desiring to interfere but slightly with the transit of the naturally conducted impulse from the body of the auricle along the line of the auricular appendix to its tip, we devised, and at first used, a pneumatic clamp. The jaws of this clamp were rigid, but one was covered by a flexible rubber membrane which could be ballooned against its fellow at varying pressures. The pressures employed

* On two occasions the chief observation of this section has been successfully carried out on the left appendix.

varied up to and somewhat beyond 300 mm. Hg ; but we were disappointed to find that such grades of compression failed to produce the desired effect, namely, an impaired conduction through the tissues of the bridge. It became obvious that the degree of compression required to produce block of different degrees could not be attained conveniently by means of pneumatic compression ; a solid metal clamp was therefore built, which would submit the muscle to much higher pressures. The jaws of this clamp were 1 centimetre wide, flat, and smooth, one jaw being moved to meet its fellow by a very fine screw having 60 threads to the inch.

The method of experiment is as follows :—Dogs of about 10 kilogrammes weight are employed and these are fully anæsthetised with morphia, paraldehyde and ether. The heart is exposed, the tip of the right appendix secured and passed through the jaws of the clamp, until the latter rests at the base of the appendix. The tip of the appendix is then fastened without material tension to a convenient part of the chest wall, and the clamp secured to an adjustable stand. Two pairs of non-polarisable contacts are now placed in the line of the auricular appendix, one pair lying proximal and the other distal to the clamp ; gaps of about a centimetre being allowed between the edges of the clamp and the nearest contacts, to avoid disturbance of the contacts on tightening the clamp. Each pair of non-polarisable contacts is connected to one string of the recording galvanometer. A pair of stimulating electrodes is placed on the body of the right auricle, and in line with the two pairs of recording contacts, and into these rhythmic induction shocks are sent, at a rate slightly surpassing the rate of the natural heart beat after section of the two vagi. To these rhythmic shocks, which are maintained throughout the experiment, the auricle responds, and with each response the excitation wave passes to the proximal contacts, across the area involved by the clamp and to the distal or appendicular contacts ; the arrival of the wave at the two pairs of contacts is thus recorded, and the corresponding transmission intervals are subsequently measured.

By graduating the clamp pressure it is easy to obtain various grades of block between the body of the auricle and the appendix. The first change observed on tightening the clamp is a widening of the transmission interval ; this widening increases until the auricular appendix occasionally fails to respond ; with more severe pressure this failure to respond becomes more frequent, 2 : 1 block becomes established, and finally, with heavy pressure, no beats are transmitted.

At any of these stages, the effect of vagal stimulation upon the block so induced may be tested. It is to be observed, however, that if pressure is applied and a certain grade of block is obtained, maintenance of this same pressure for unduly long periods of time is accompanied by an increase in the grade of block ; the pressure used is much more than is sufficient to bring the blood supply to the appendix to an end, and the muscle will not continue for many minutes to beat in these circumstances. It is necessary, therefore, by preliminary tests, to gain an idea of the pressure needed to

produce a desired grade of block, and to apply this pressure without undue delay; otherwise a sufficient period of uniform block will not be obtained for the purposes of the test. A period of time sufficient for the test of vagal stimulation and subsequent recovery from this test is required. The latter is not always but is usually obtainable. A period sufficient for two complete tests is not usually attainable; it is best to withdraw the pressure as soon as the first test is complete, and to reapply it subsequently in further tests, since severe initial pressure is usually required; its early withdrawal in observations in which complete block is produced by clamping is especially desirable. For, if severe pressure is maintained unduly, recovery of conduction on removing the clamp is very slow, occupying half an hour or more. In the case of lesser grades of block, recovery on removing the clamp usually occurs within a few seconds or at the most minutes.

When the vagal stimulation affects blocks so produced it does so in an almost constant manner, it reduces the block; and this statement applies to each degree of block. The reduction of the block usually occurs promptly, and is maintained throughout stimulation. The block reappears shortly after vagal stimulation ceases.

Exceptionally vagal stimulation fails to affect the block; this happens in two circumstances. Firstly, if the vagus is inactive or is inadequately stimulated. Whether the vagus has or has not acted on the heart is known from an examination of the records; for although these records are essentially auricular records, a small and clear ventricular representation is also seen in them. This disappears under vagal stimulation, as does the ventricular beat in a simultaneous ventricular myogram, because *A-V* block becomes established. It is to be remembered that the auricular rate is being maintained at 160-210 throughout the observation, and that in this circumstance both right and left vagus yield high grades of *A-V* block. We use such strengths of vagal stimulation as will bring the ventricle to a standstill or will induce a high grade of partial *A-V* block, and this *A-V* block forms a safe control of the general influence which the vagal stimulation has exerted in each observation. Secondly, the vagal stimulation may fail to affect the block if the pressure exerted by the clamp has been too great or has been too long maintained. Such exceptions are exclusively instances of block originally complete in its degree, and in all such recovery from block on releasing the clamp has been long delayed. In such experiments failure to obtain the usual vagal effect may be due to death of the muscle fibres, though this is rarely the case, since ultimate recovery of conduction is almost invariable; it is more probably due to damage of the nerve fibres beneath the clamp. In several instances, after releasing the clamp, a complete block has been maintained for periods of many minutes and even of 40 minutes, yet at any time during this period the block could at once be broken down temporarily to a 1:1 response by stimulating the vagus (Dog NY, record No. 16). In a solitary instance (Dog NZ, record No. 3) a slightly prolonged interval (*A-A* was not reduced by effective vagal

stimulation; in a solitary instance (Dog NX, record No. 3) a prolonged interval was slightly increased by vagal stimulation. For these two minor exceptions we have no explanation to offer.

Reduction in the degree of block is produced by stimulating either the right and left vagus, and in our experiments the two nerves have seemed equally effective in this respect.

Complete abolition of the block is not usually seen, though the block is almost abolished. Thus, although complete block is always reduced to a condition in which there is invariable response, yet the short original transmission interval is not generally reached. It may be reached, and is often almost reached, but even at the height of the reaction, the intervals usually remain a little lengthened. Failure to reduce the block entirely is evidently due, in large measure at all events, to damage produced by the clamp. After clamping and releasing the muscle, the original intervals are not usually entirely restored; if time is allowed, recovery occurs but is rarely quite complete. It would appear that conduction, depressed by clamping, is restored or greatly improved by vagal stimulation; when under vagal stimulation a slight defect still remains, it may be ascribed in part at least, to permanent damage of the tissue, perhaps through interference with its blood supply.

The after-effects of vagal stimulation as opposed to the effects witnessed during stimulation, are more difficult to study. Usually the degree of block preceding vagal stimulation reappears; but the after-effects are not infrequently complicated by increase in the grade of block consequent on the clamp pressure being maintained; for the effect of the clamp is the establishment of a certain grade of block, which after a time tends to increase if pressure is continued.

These observations are illustrated by records and by Table I. In Fig. 1 the top curve (*V.M.*) is a ventricular myogram, in which the beats of the ventricle (*v*) are clearly shown. The centre curve (*APP*) is an electrogram from the appendix distal to the clamp; the lowest curve is an electrogram from the body of the auricle, proximal to the clamp. Throughout the record the clamp was on; the body of the auricle is beating in response to rhythmic shocks, entering it at a rate of 167 per minute, as shown by the sharp deflections in the lowest curve; the ventricle is responding to the auricle at the same rate, its movements being recorded by the myograph and by the small deflections *v* in the lowest curve. On the other hand, the appendix is not responding; complete block between it and the body of the auricle exists. Shortly after vagal stimulation begins the ventricle stops beating, and almost immediately the appendix responds for the first time (beat 5); the appendix fails to respond to the next impulse (beat 6), but responds regularly to impulses 7, 8, 9, 10, etc.. Thus, while the vagal stimulation produces a profound degree of block at the *A-V* junction, it quickly relieves the block previously produced at the base of the auricular appendix by the clamp.

TABLE I.
Influence of vagal stimulation upon intra-auricular block produced by compression.

Dog.	Record No.	Con- trolled auric. rate.	Conduction.		Vagus.	Coil at	Simultaneous effect on A-V conduction.	Remarks.
			Before stimulation.	During stimulation.				
NV	2	187	1:1 (A-A*=0.0589)	1:1 (A-A=0.0503)	right	5.0 cm.	9:1, 4:1, 3:1	Clamp reapplied.
	4	187	3:1	1:1 (A-A=0.0516)	right	5.0 cm.	3:1	Clamp reapplied.
	5	187	3:1	1:1 (A-A=0.0570)	right	5.0 cm.	3:1, 2:1, 3:1, 3:1	Clamp reapplied.
	6	185	4:1	1:1 (A-A=0.0705)	right	5.0 cm.	3:1	Clamp reapplied.
	7	185	2:1	1:1 (A-A=0.0754)	left	5.0 cm.	5:1, 4:1	7 mins. after releasing clamp.
	8	187	2:1	1:1 (A-A=0.0660)	left	5.0 cm.	4:1, 2:1, 2:1	9 mins. after releasing clamp.
	2	200	Complete block	1:1 (A-A=0.0604)	right	5.0 cm.	Standstill of ventricle	Clamp reapplied.
	3	200	"	1:1 (A-A=0.0449)	right	5.0 cm.	"	3 mins. after releasing clamp.
NW	4	200	"	1:1 (A-A=0.0534)	right	5.0 cm.	"	Clamp reapplied.
	5	200	2:1 (A-A=0.0622)	1:1 (A-A=0.0600)	right	6.0 cm.	"	Clamp reapplied.
	6	200	2:1 (A-A=0.1181)	1:1 (A-A=0.0559)	left	5.5 cm.	4:1, 4:1, 6:1	Clamp reapplied.
	2	180	1:1 (A-A=0.0317)	1:1 (A-A=0.0469)	—	—	—	Before clamping.
	3	183	1:1 (A-A=0.0400)	—	right	5.0 cm.	3:1, 2:1, 2:1, 2:1	Clamp applied.
	4	180	1:1 (A-A=0.0330)	—	—	—	—	2 mins. after clamp released.
NX	5 & 6	187	Complete block	Complete block	right	5.0 cm.	2:1	Clamp reapplied.
	8	187	Occ. dropped beat	1:1 (A-A=0.0609)	right	4.5 cm.	2:1	Clamp reapplied.
	9	206	1:1 (A-A=0.0362)	—	—	—	—	11 mins. after clamp released.
	10	210	2:1 (A-A=0.1150)	2:1 (A-A=0.0930)	right	4.0 cm.	5:1, 3:1	Clamp reapplied.
	11	208	Complete block	Complete block	right	4.0 cm.	4:1, 4:1, 3:1	4 mins. after clamp released.
	12	208	"	2:1	left	4.0 cm.	5:1, 4:1, 3:1, 3:1	Clamp reapplied.
	13	205	"	Complete block	left	4.0 cm.	5:1, 6:1, 4:1, 3:1	Clamp reapplied.
	14	200	"	1:1 (A-A=0.0544)	left	4.0 cm.	5:1	Clamp reapplied.
	15	205	"	2:1, later 1:1	left	4.0 cm.	6:1	Clamp reapplied.
	16	160	V. occ. responses	1:1 (A-A=0.0373)	left	4.0 cm.	5:1, 7:1	10 mins. after clamp released.

* A-A = Conduction interval between auricular contacts.

TABLE I.—*continued.*

Dog.	Record No.	Con- trolled auric. rate.	Conduction.		Vagus.	Coil at	Simultaneous effect on A-V conduction.	Remarks.
			Before stimulation.	During stimulation.				
NX— <i>cont.</i>	17	158	Complete block	1 : 1 (A-A = 0.0367)	right	4.0 cm.	6 : 1, 5 : 1	11 mins. after clamp released.
	18	158	6 : 1	1 : 1 (A-A = 0.0406)	right	4.0 cm.	6 : 1	16 mins. after clamp released.
	19	177	1 : 1 (A-A = 0.0400)	—	—	—	—	21 mins. after clamp released.
	20	165	Complete block	1 : 1 (A-A = 0.0836)	left	4.0 cm.	6 : 1, 5 : 1	Clamp reapplied.
	21	163	1 : 1 (A-A = 0.0425)	—	—	—	—	29 mins. after clamp released.
	22	167	Complete block	2 : 1, later 1 : 1 (A-A = 0.0742)	right	—	6 : 1, 5 : 1	Clamp reapplied.
	23	167	1 : 1 (A-A = 0.0411)	—	—	—	—	12 mins. after clamp released.
NY	1	172	1 : 1 (A-A = 0.0303)	—	—	—	—	Before clamping.
	2	172	Complete block	1 : 1 (A-A = 0.0558)	right	5.5 cm.	Standstill of ventricle	Clamp applied.
	3	172	1 : 1 (A-A = 0.0348)	—	—	—	—	7 mins. after releasing clamp.
	3a	174	Complete block	1 : 1 (A-A = 0.0742)	left	5.5 cm.	Standstill of ventricle	Clamp reapplied.
	4	172	2 : 1 (A-A = 0.0798)	1 : 1 (A-A = 0.0733)	right	5.5 cm.	" "	Clamp reapplied.
	5	174	1 : 1 (A-A = 0.0512)	—	—	—	—	2 mins. after releasing clamp.
	6	172	Complete block	1 : 1 (A-A = 0.0568)	left	5.5 cm.	4 : 1	Clamp reapplied.
	7	173	1 : 1 (A-A = 0.0504)	—	—	—	—	7 mins. after releasing clamp.
	11	176	1 : 1 (A-A = 0.0612)	—	—	—	—	Clamp reapplied. Re-cord 5 mins. after releasing clamp.
	12	175	Complete block	1 : 1 (A-A = 0.0599)	right	4.5 cm.	Standstill of ventricle	About 3 mins. after release of clamp.
	13	175	" "	1 : 1 (A-A = 0.0625)	left	4.5 cm.	" "	5 mins. after release of clamp.
	16	175	" "	1 : 1 (A-A = 0.0260)	right	5.5 cm.	4 : 1, 4 : 1, 4 : 1, 2 : 1	40 mins. after release of clamp (repeated several times).
	17	175	" "	1 : 1 (A-A = 0.0444)	right	5.5 cm.	Standstill of ventricle	—
	18 & 19	180	1 : 1 (A-A = 0.0659)	1 : 1 (A-A = 0.0485)	right	5.5 cm.	" "	58 mins. after re-leasing clamp.

	20	180	Complete block	1:1 (A-A=0.0420)	right	4.5 cm.	"	"	10 mins. after releasing clamp. Same effect repeated 5 times during next 10 mins. Effect abolished by atropine.
NZ	2	175	1:1 (A-A=0.0321)	1:1 (A-A=0.0412)	right	6.0 cm.	Standstill of ventricle	Before clamping.	Clamp applied.
	3	175	1:1 (A-A=0.0407)	—	—	—	—	4 mins. after releasing clamp.	Clamp reapplied.
	4	175	1:1 (A-A=0.0375)	—	right	6.0 cm.	High grade of block	4 mins. after releasing clamp.	Clamp reapplied.
	5	177	1:1 (A-A=0.0574)	1:1 (A-A=0.0543)	right	6.0 cm.	High grade of block	4 mins. after releasing clamp.	Clamp reapplied.
	6	179	1:1 (A-A=0.0479)	—	right	5.0 cm.	2:1, 8:1	4 mins. after releasing clamp.	Clamp reapplied.
	7 & 9	179	2:1	1:1 (A-A=0.0718)	right	6.0 cm.	High grade of block	4 mins. after releasing clamp.	Clamp reapplied.
	16	180	1:1 (A-A=0.0788)*	—	right	5.0 cm.	1:1, 3:1, 5:1	Clamp reapplied.	Clamp reapplied.
	17	182	1:1 (A-A=0.0596)	—	right	5.0 cm.	—	Clamp reapplied.	Clamp reapplied.
	18	185	1:1 (A-A=0.0705)	1:1 (A-A=0.0647)	right	5.0 cm.	—	Clamp reapplied.	Clamp reapplied.
	1	172	1:1 (A-A=0.0316)	—	—	—	—	Before applying clamp.	Clamp applied.
OB	2	172	1:1 (A-A=0.0588)	1:1 (A-A=0.0512)	right	4.5 cm.	2:1, 2:1, 2:1	2½ mins. after clamp released.	Clamp reapplied.
	3	171	1:1 (A-A=0.0370)	—	right	4.5 cm.	2:1, 2:1, 2:1	3 mins. after clamp released.	Clamp reapplied.
	4	171	Very occ. response	1:1 (A-A=0.0535)	right	4.5 cm.	2:1, 2:1, 2:1	6 mins. after clamp released.	Clamp reapplied.
	5	172	1:1 (A-A=0.0408)	—	left	4.5 cm.	—	Clamp reapplied and released; observation repeated and same effect obtained.	After injection of atropine, other conditions unaltered.
	6	172	1:1 (A-A=0.0531)	1:1 (A-A=0.0370)	right	4.5 cm.	Heart block	Same repeated with right and left vagus with similar results.	24 mins. after clamp released.
	7	171	1:1 (A-A=0.0369)	—	right	4.5 cm.	No block	Clamp reapplied.	Clamp reapplied.
		171	Complete	1:1	right	4.5 cm.	No block	Clamp reapplied.	Clamp reapplied.
		172	Complete	Complete	right	4.5 cm.	No block	Clamp reapplied.	Clamp reapplied.
	10	172	1:1 (A-A=0.0793)	1:1 (A-A=0.0471)	right	4.5 cm.	No block	Clamp reapplied.	Clamp reapplied.
	12	172	Very occ. response	Very occ. response	right	4.5 cm.	No block	Clamp reapplied.	Clamp reapplied.

* This interval (and those which follow) is not comparable with those which precede it in the same column, the contacts having been moved.

TABLE II.

Influence of vagal stimulation upon intra-auricular block produced by cooling.

Dog.	Record No.	Controlled auric. rate.	Temperature.	Conduction.		Effect on A-V conduction.	Vagus.
				Before stimulation.	During stimulation.		
OM	26	175	36°C	1:1 (A-A=0.0585)	1:1 (A-A=0.0576)	Standstill of ventricle	Right
	25	178	30°C	1:1 (A-A=0.0625)	1:1 (A-A=0.0619)	"	"
	24	176	25°C	1:1 (A-A=0.0700)	1:1 (A-A=0.0623)	"	"
	22	176	20°C	1:1 (A-A=0.0737)	1:1 (A-A=0.0652)	"	"
	21	177	20°C	1:1 (A-A=0.0805)	1:1 (A-A=0.0670)	"	"
	19	177	14°C	2:1 (A-A=0.0863)	1:1 (A-A=0.0779)	"	"
ON	5	176	35°C	1:1 (A-A=0.0307)	1:1 (A-A=0.0269)	"	"
	6	175	29°C	1:1 (A-A=0.0324)	1:1 (A-A=0.0304)	"	"
	7	176	25°C	1:1 (A-A=0.0358)	1:1 (A-A=0.0330)	"	"
	8	177	20°C	1:1 (A-A=0.0452)	1:1 (A-A=0.0380)	"	"
	9	177	15°C	1:1 (A-A=0.0523)	1:1 (A-A=0.0409)	"	"
	10	177	15°C	$\left\{ \begin{array}{l} 1:1 (A-A=0.0499)^* \\ 1:1 (A-A=0.0355)^{\dagger} \end{array} \right\}$	1:1 (A-A=0.0419) [‡]	"	"
	11	176	13½°C	2:1 (A-A=0.0534)	1:1 (A-A=0.0449)	"	"
	17	177	10°C	Complete block	1:1 (A-A not measurable)	"	"
	19	175	35°C	1:1 (A-A=0.0265)	1:1 (A-A=0.0266)	"	"
	20	175	30°C	1:1 (A-A=0.0288)	1:1 (A-A=0.0260)	"	"
	21	176	25½°C	1:1 (A-A=0.0297)	1:1 (A-A=0.0293)	"	"
	22	174	20°C	1:1 (A-A=0.0315)	1:1 (A-A=0.0302)	"	"
	24	175	16°C	1:1 (A-A=0.0352)	1:1 (A-A=0.0320)	"	"
	25	174	12°C	1:1 (A-A=0.0379)	1:1 (A-A=0.0339)	"	"
	27	175	10°C	2:1 (A-A=0.0418)	1:1 (A-A=0.0334)	"	"

OOa	3	180	35°C	1:1 (A-A=0.0417)	1:1 (A-A=0.0414)	4:1 occas. 2:1§	Right
	4	180	30°C	1:1 (A-A=0.0415)	1:1 (A-A=0.0397)	4:1 occas. 2:1	"
	5	178	25°C	1:1 (A-A=0.0453)	1:1 (A-A=0.0415)	4:1 occas. 3:1	"
	7	182	20°C	1:1 (A-A=0.0564)	1:1 (A-A=0.0556)	4:1 occas. 2:1	"
	8	179	20°C	1:1 (A-A=0.0606)	1:1 (A-A=0.0592)	4:1 occas. 2:1	"
	9	180	15°C	2:1 (A-A=0.0750)	1:1 (A-A=0.0920)	4:1 occas. 2:1	"
	10	178	15°C	2:1 (A-A=0.0736)	2:1 (A-A=0.0618)	4:1, 2:1, 1:1	"
OOb	2	154	35°C	1:1 (A-A=0.0673)	1:1 (A-A=0.0658)	4:1, 3:1	Right
	3	154	30°C	1:1 (A-A=0.0652)	1:1 (A-A=0.0660)	4:1, 3:1	"
	4	156	25°C	1:1 (A-A=0.0829)	1:1 (A-A=0.0840)	4:1	"
	5	156	20°C	1:1 (A-A=0.0928)	1:1 (A-A=0.0850)	4:1	"
	9	156	15°C	2:1 (A-A=0.1161)	1:1 (A-A=0.0999)	4:1	"
	14	152	20°C	2:1 (A-A=0.0967)	1:1 (A-A=0.0883)	4:1	"
	15	150	25°C	1:1 (A-A=0.0810)	1:1 (A-A=0.0755)	4:1, 3:1	"
	16	152	25°C	1:1 (A-A=0.0777)	1:1 (A-A=0.0743)	4:1	"
OQ	3	158	35°C	1:1 (A-A=0.0262)	1:1 (A-A=0.0268)	Standstill of ventricle	Right
	4	156	30°C	1:1 (A-A=0.0253)	1:1 (A-A=0.0258)	"	"
	5	158	25°C	1:1 (A-A=0.0260)	1:1 (A-A=0.0273)	"	"
	6	158	20°C	1:1 (A-A=0.0275)	1:1 (A-A=0.0304)	"	"
	7	158	15°C	1:1 (A-A=0.0431)	1:1 (A-A=0.0400)	"	"
	9	160	12½°C	2:1 (A-A=0.0465)	1:1 (A-A=0.0423)	"	"
	10	160	13°C	2:1 (A-A=0.0440)	2:1 (A-A=0.0425)	"	"
	11	159	13°C	2:1 (A-A=0.0440)	2:1 (A-A=0.0415)	"	"
	15	159	14°C	2:1 (A-A=0.0397)	1:1 (A-A=0.0580)	"	"
	18	159	14°C	2:1 (A-A=0.0370)	1:1 (A-A=0.0560)	"	"

* Heavy alternation.

† Alternation abolished.

‡ Allowed to recover contacts moved and following records taken.

§ Right vagal stimulation 4:1 block was produced which immediately gave place to a 2:1, and often 1:1 with prolonged P.R.

A second and very similar record is shown in Fig. 2. In this record the clamp had been released from the auricle for 40 minutes, during which time complete block was always present, except when the heart was under vagal stimulation (see Table I). In this the relief of the block is more prompt, as is usual, and a 1:1 response of the appendix is established, without the interposition of a 2:1 period. Meanwhile the ventricle is brought to a temporary standstill. As the heart recovers from the effect of stimulation, the auricular block reasserts itself and the appendix again becomes motionless.

A series of observations is tabulated in Table I, where under "controlled auricular rate" the rate of rhythmic response to stimulation maintained during the whole of the corresponding observation is given. In the next two columns conduction from auricle to appendix before and during vagal stimulation is indicated by the ratio of the rates, and in the case of 1:1 response by the transmission intervals ($A-A$). In the succeeding columns the vagus used and the strength of stimulation are indicated. In the last column but one the degree of $A-V$ block resulting from vagal stimulation is noted. In the last column the relation of the observation to the application or release of the clamp is indicated. Most of the observations were made immediately after the first application of the clamp, or after its release and re-application.

Atropine and acetyl-choline. That the effect on the auricular block is a true vagal effect and is not due to escape of current to the sympathetic has been fully determined. The vagus (right and left) was stimulated high in the neck in all instances; in two experiments (Dogs NY and OB), after repeatedly obtaining release of the appendix from a condition of persistent complete block, atropine was injected intravenously, without reapplying the clamp. The reaction was in each case destroyed by this injection, the adequacy of which was shown by the simultaneous disappearance of vagal block at the $A-V$ ring. More recently instead of faradising the vagus, we have used acetyl-choline to stimulate it, and have obtained an identical reaction, namely, release of high grades of block produced by clamping.

Observations on block produced by cooling.

We first attempted to obtain intra-auricular block as a result of cooling, by means of a specially constructed cooler. The apparatus consisted of a small circular box of brass, flat on its upper and lower surfaces and having a circular hole cut through its centre to expose a corresponding area of muscle to view when the box lay flat on the auricular wall. The sides of this hole were sealed off with metal, so as to convert the rest of the box into a closed and hollow brass ring; into the latter, inlet and outlet tubes were soldered, and through these water at various temperatures could be passed. Thus, a central area of muscle could be examined while the surrounding ring of muscle could be cooled at will. It was hoped that by passing water sufficiently

cold through the ring, a block between outer and inner muscle could be induced, while the former responded to rhythmic stimulation. This procedure was not successful, however, for in only one out of a number of experiments could such block be obtained. The difficulty, so it was judged, was that deep muscle fibres were apt to escape cooling on one or other side of the ring. The method was abandoned.

Eventually we succeeded by using again the base of the appendix. With a powerful clamp the muscle bounding the deep surface of the appendix at its base was crushed and destroyed, and this line of crush was prolonged on to the superficial surface of the appendix, so that only a small bridge of muscle, $\frac{1}{2}$ to 1 cm. across, joined the body of the auricle to the appendix itself. A flat lead tube was laid on this bridge, and water, at various temperatures, was passed through it. Pairs of contacts were arranged, as in the previously described experiments, one on the appendix and one on the body of the auricle, and the auricle was stimulated in line with these.

Effect of cooling. Records were taken while the water was at body temperature, and at temperatures varying from this down to $10^{\circ}\text{C}.$, the water being allowed to circulate for 2 minutes on each occasion. The transmission interval is on occasion found to rise when the temperature falls below 30° or 25° , usually, when it falls below 20° . This rise of interval increases until a temperature of about 15° is reached, when, if the auricle is beating at rates of about 150-180 per minute, 2:1 response appears (see Table II). Before the appearance of 2:1 response, the transmission interval has risen by approximately 50 per cent. On one occasion, complete block was seen at a temperature of 10° .

Effect of vagal stimulation. The right nerve has alone been tested. When an effect is produced, it is uniformly expressed as a reduction in the degree of the preceding block. The instance of complete block and most instances of 2:1 block could thus speedily be reduced to a condition of 1:1 response. The reaction, however, takes place after a rather longer delay than is the case with compression block. When, under cooling, a 1:1 response, accompanied by a prolonged transmission interval, prevails, vagal stimulation reduces the length of this interval. Where the original prolongation is slight, under the influences of the vagus it becomes normal again. Where the prolongation is greater, the interval is very decidedly reduced but does not return to the normal figure.

In some experiments, however, especially in those where temperatures of $14^{\circ}\text{C}.$ and lower are being used, no decided effect may be witnessed upon stimulating the vagus. This can be seen from Table II, when in the 2:1 block stage, vagus stimulation fails frequently to relieve the block, or to show any material reduction in the transmission intervals.

It is to be remarked that we are also cooling nerves and nerve endings, and that the cooling must spread into the muscle surrounding the lead tube,

and that this failure to elicit a reaction to vagus stimulation may be due to a consequent local failure of the nerve endings. That spread of cooling is taking place is indicated by the intrinsic deflections, given by the distal electrodes, placed upon the tip of the appendix. These intrinsic deflections, as the temperature in the tube is lowered, begin to lose their original form, present a much less sharp rise and fall, and a smaller amplitude; suggesting that changes are taking place both in the systole of the muscle underlying the electrodes and in conduction; alternation is frequently met with while these changes are progressing, and such alternation is abolished by vagal stimulation.

Fig. 3 shows a record of a 2 : 1 block passing into a 1 : 1 response under vagal stimulation. The top curve (*APP*) is an electrogram from the appendix distal to the clamp, and the bottom curve (*AUR*), from the body of the auricle proximal to the clamp. At the beginning of the record, water at a temperature of $12\frac{1}{2}^{\circ}\text{C}$. has been flowing through the tube for 2 minutes, and the body of the auricle is responding to rhythmic shocks at the rate of 159 per minute, and gives rise to the sharp deflections of the lower curve; the ventricle is responding to the auricle and is recorded as small deflections (*v*) in the lower curve. The tip of the appendix is responding to every alternate stimulus, and gives rise to the deflections in the upper curve (which are less sharp than in the lower curve). The vagus is then stimulated just after beat 1, and the ventricle is brought to a standstill, and shortly afterwards, from beat 8 onwards, the appendix responds to every stimulus.

Although in these effects the vagus was stimulated high up in the neck, it seemed desirable that this result of vagal stimulation should be confirmed by the injection of acetyl choline; sufficient acetyl choline was injected to produce a complete ventricular standstill, and in this way also the 2 : 1 block was relieved several times.

Discussion.

The observations here recorded were largely prompted by previous work in which the conclusion has been reached that the vagus has no effect on the rate of *fibre* conduction in the normally beating auricle, but that when, in special circumstances, conduction through the muscle sheet is impaired, vagal stimulation is capable of restoring normal conduction. Impairment of auricular conduction, consequent on a high rate of beating, or after the administration of such poisons as strophanthin and quinidine, is relieved partially or completely by vagal stimulation. This effect has been ascribed to the power of the vagus to reduce the length of the refractory period of the auricular muscle, an increase of the latter being in the circumstances largely or wholly responsible for the originally defective conduction. By provoking intra-auricular block, either by pressure or by cooling, we had hoped to add further examples of a parallel kind, and thus to establish our conclusions on a more general basis.

The first anticipation has not been disappointed, for both by pressure and by cold, block may be produced in its several degrees in the auricular muscle ; and these blocks, like those previously dealt with, are cleared away in part or in whole by vagal stimulation. This result was anticipated, because it was thought probable⁷ that compression and cold might induce block, either by prolonging the systole of the muscle, and thus lengthening its refractory period, or by depressing excitability. The second hope, that our former conclusions might be made general, has not been fulfilled completely.

Prolonged conduction intervals and 2:1 response might be explained on the basis of a prolonged refractory period, or by a lowered rate of recovery of excitability, when they are produced by cold or pressure. A relief of blocks, so arising, by vagal stimulation could be explained reasonably, by supposing a reduction of the refractory period with its consequent lengthening of the period of recovery. But we have encountered unexpectedly the fact that complete block, produced by the same means, is also relieved. The case which presents the greatest difficulty is that of complete block produced by pressure. In this instance, the muscle pressed upon may refuse to conduct for very long periods, extending to as long as 40 minutes and persisting long after removal of the clamp. The muscle is not dead, for it will recover after this long period of quiescence ; neither is it rendered temporarily and wholly incapable of functioning ; for if at any time during this period the vagus is stimulated the obstruction to the passage of impulses is removed for the period of stimulation. The remarkable fact remains that the functions of the compressed muscle appear to lie dormant for considerable periods of time, and that the vagus is capable of throwing them once more into activity. To explain blocks of this kind as resulting from lengthened refractory period, and their removal by the vagus as due to the shortening of the refractory period, would involve two distinct assumptions ; firstly, that severe pressure can produce a contraction in muscle of inordinate duration, a form of prolonged standstill in systole, and, secondly, that vagal stimulation is capable of reducing the length of a systole during its progress. In regard to the last assumption, we know of neither supporting nor conflicting evidence ; but the correctness of the first assumption appears so improbable that, for the moment at all events, it must be placed on one side.

A curious and paradoxical acceleration of the whole heart occurring in special circumstances and under vagal stimulation has been recorded by Dale, Laidlaw and Symons¹; they inclined to attribute it to the presence of normal cardiac accelerators in the vagal as opposed to sympathetic fibres, their idea being that the effect of stimulating these accelerator fibres is normally overshadowed by that of the inhibitor fibres. They regarded the condition of their experiments as producing a depression of the inhibitory fibres, thus revealing the accelerator effects. The reactions which we have described are not susceptible to a like explanation ; for they are invariably

accompanied by a profound inhibitory action upon other parts of the heart ; when the local block at the base of the appendix is relieved, a high grade of block is simultaneously manifested at the *A-V* junction and, as is readily seen in the experiments, the auricular contractions diminish almost to the point of invisibility. Thus it is quite clear that the inhibitory vagal fibres are exercising their usual profound influence upon the heart as a whole, at the instant at which the block is relieved in the appendix ; and we are consequently indisposed to accept the view that the local effect results from a selective action of accelerator vagal fibres, which might be supposed to exist. It appears to us that we have to deal with a normal vagal impulse, playing upon muscle in which the conditions are peculiar ; and that this local peculiarity of the muscle fibres (consequent on pressure or cooling) is responsible for the effect witnessed. We go farther and suggest that the phenomenon brought to light in this fashion may be the revealing of normal effects of vagal governance of the heart, effects always present but usually concealed. It is to be emphasised that we are not able to exclude an action comparable or analogous to that previously described, where a reduction of the refractory period of the muscle produces an apparently paradoxical effect ; but given that such an explanation is inapplicable to the present effects, then we are thrown back upon more fundamental inferences. Gaskell⁶ was wont to lay stress upon the anabolic effect of vagal stimulation. Of the precise view which he held we feel uncertain. It is clear, however, that he intended to express an activity contrary in its direction to that displayed as a depression of function, and that he considered the vagus may be responsible for a building up and storing of energy, though its activity is chiefly displayed in preventing the dispersal of energy. These ideas of his do not appear at any time to have gained wide acceptance, and some of the arguments which he used to support them have since weakened. The most notable instance of this weakening of evidence is to be found in Einthoven's² recent explanation of Gaskell's experiment,⁶ in which he described a positive variation of the demarcation current under vagal stimulation. Gaskell regards the nerve supplying a somatic muscle as katabolic, and the vagal supply of the heart as anabolic ; he instances the positive variation produced by the vagus in contradistinction to the negative variation of the demarcation current produced by the somatic nerve. It seems probable from Einthoven's observations that this positive variation, induced by vagal stimulation, is non-existent. That being the case, we are led to inquire if evidence from other sources supports the view that vagal stimulation leads to a building up and storage of energy, while at the same time it impedes its dispersal in the form of muscular activity. Of a storage there is evidence ; of a building up which is more intense than normal, there is little evidence that is clear. Yet, because this evidence is unclear the hypothesis cannot be placed altogether on one side ; it might be used to explain the phenomena which we have been describing. Our suggestion is that in the circumstances of our own experiments the vagal influences

which may be exerted normally upon the energy of the muscle, namely, an increased storage on the one hand and a diminished dispersal on the other, become locally dissociated; that the first is retained and that the last is decreased or abolished. A parallel explanation appears to us to be applicable to the phenomena described by Dale, Laidlaw and Symons, as an alternative to that put forward by these workers.

CONCLUSIONS.

1. Block in varying degrees can be produced between different portions of the auricular muscle of the dog by applying pressure or cold.

2. The blocks so produced are abolished in part or in whole by stimulating the vagus, while simultaneously the inhibitory nerve influence is displayed at the *A-V* junction by the production of block.

3. The meaning of this paradox is discussed.

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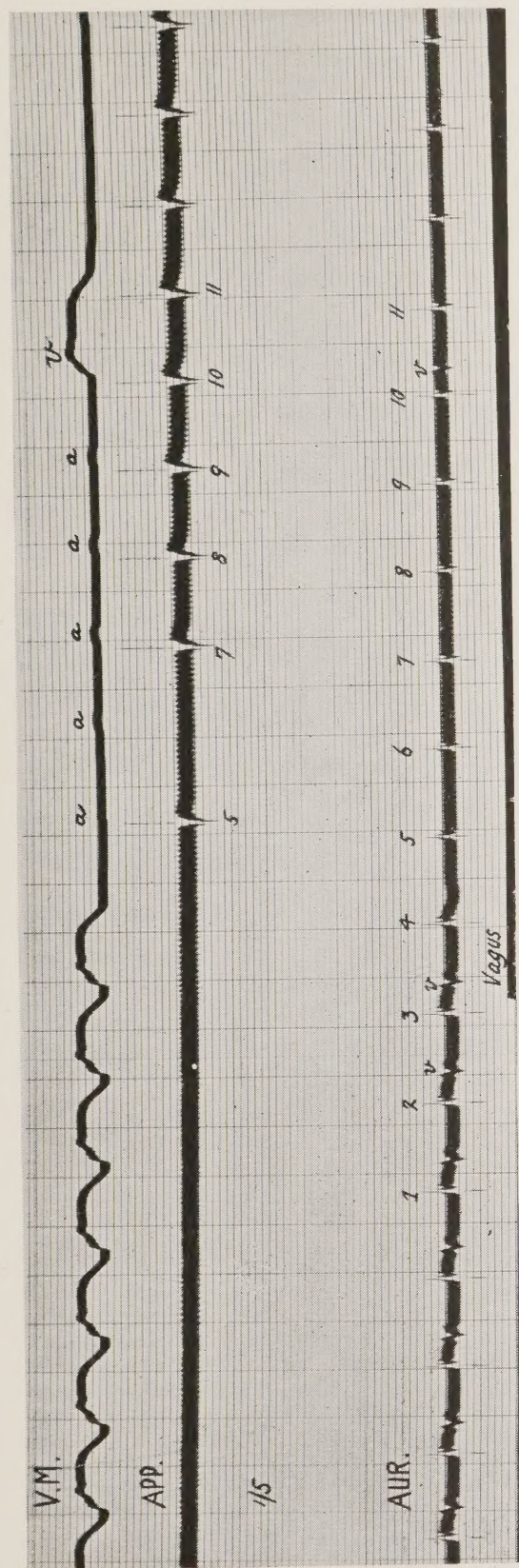


Fig. 1. (Dog NX, record No. 22.) V.M.=ventricular myogram. APP.=right appendicular and AUR.=auricular electrogram. Complete block between the auricle and appendix, recently produced by clamping the base of the appendix, is relieved by stimulating the right vagus. The vagal stimulation produces standstill of the ventricle. Time in fifths of a second in this and the remaining records.

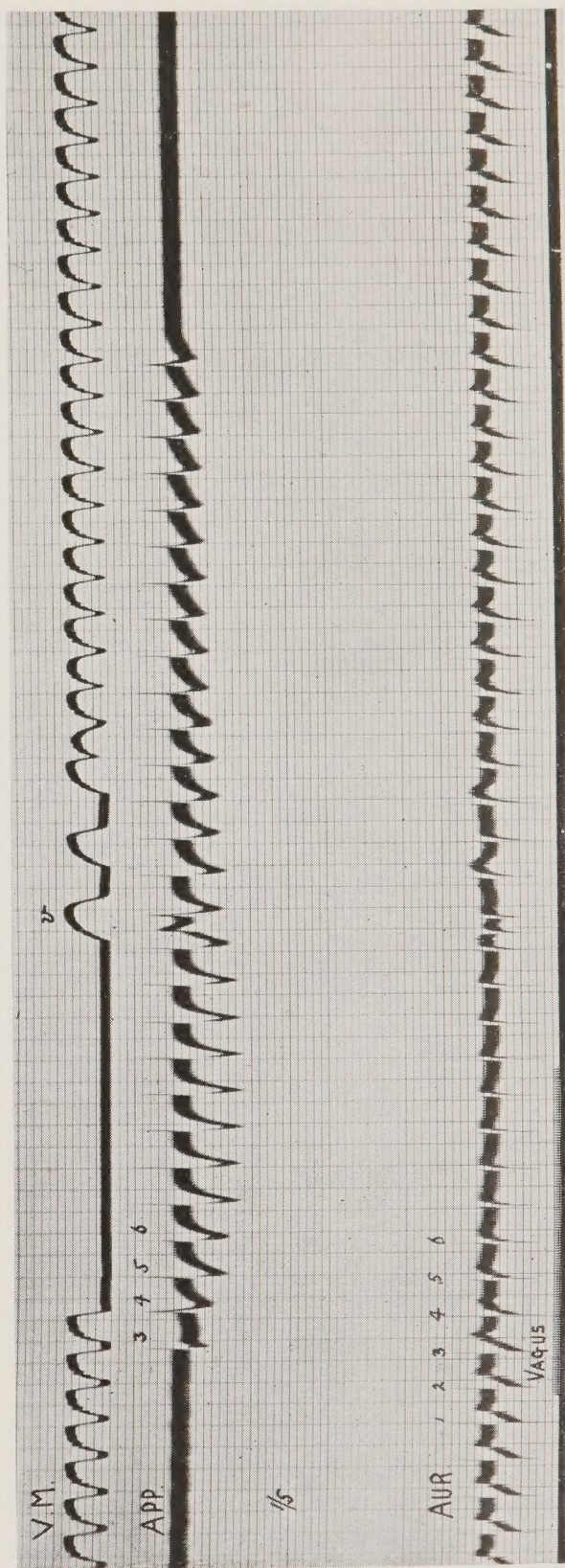


Fig. 2. (Dog NY, record No. 17.) A similar record, showing the relief of complete block by right vagal stimulation, and the subsequent reappearance of complete block. The record was taken 40 minutes after releasing the clamp.

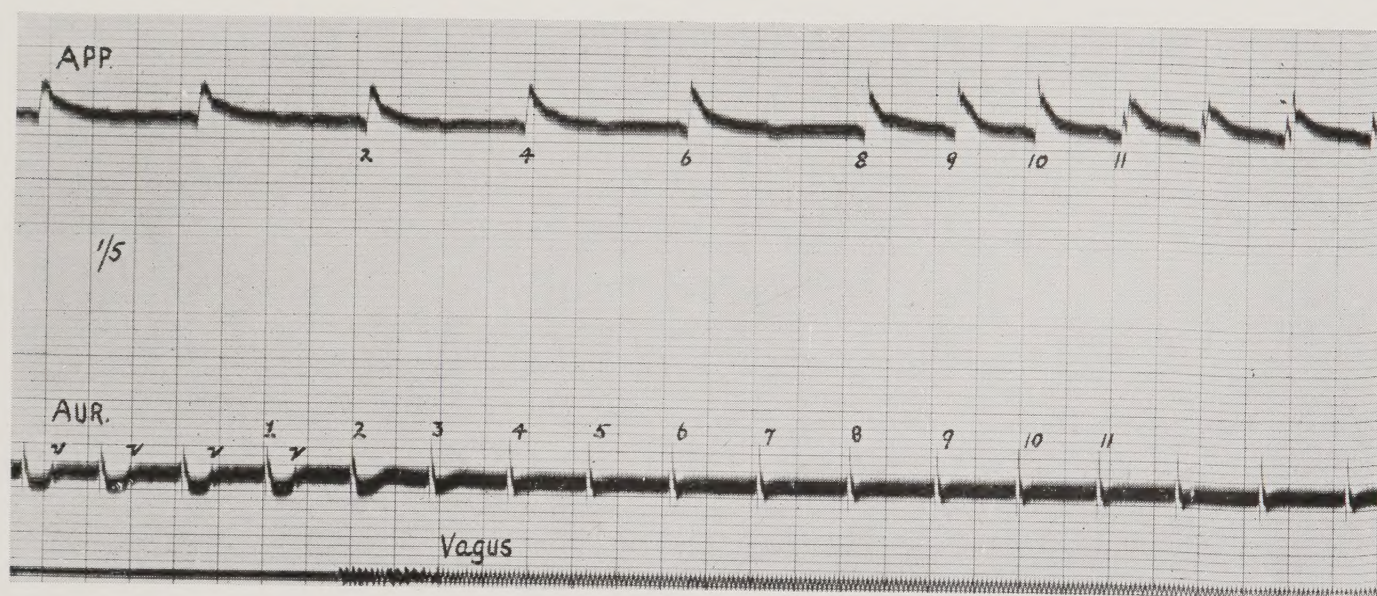


Fig. 3. (Dog OQ, record No. 9.) *APP.*=appendicular and *AUR.*=auricular electrogram. 2 : 1 block between auricle and appendix has been produced by cooling the base of the appendix to $12\frac{1}{2}^{\circ}\text{C}$. Right vagal stimulation soon converts the 2 : 1 into a 1 : 1 response, which continues to the end of the record.

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